IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Gonda et al.
Serial No.	:	09/848,774
Filed	:	May 3, 2001
For	:	A METHOD OF TREATING DIABETES MELLITUS IN A PATIENT
Examiner	:	Aaron J. Lewis
Group Art Unit	:	3761

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APPEAL BRIEF

Sir:

Applicants hereby appeal the final rejection of the claims presently pending in the above-referenced application and set forth below their bases for this appeal. Enclosed with this Appeal Brief are: (1) the brief fee of $330.00; (2) an Amendment under 37 C.F.R. § 1.116 canceling certain claims and making corrections of a typographical nature in the remaining claims to facilitate this appeal; and (3) a petition for a five month extension of the period for response and the respective fee of $2010.00.

(1) REAL PARTY IN INTEREST

The real party in interest in the above-referenced application is Aradigm Corporation of Hayward, California, the owner of the application. The application is presently licensed exclusively to Novo Nordisk A/S of Bagsvaerd, Denmark, to which Aradigm Corporation is obliged to assign its rights.

(2) RELATED APPEALS AND INTERFERENCES

Appellants are not aware of any appeals or interferences related to the above-identified patent application.

(3) STATUS OF CLAIMS

This is an appeal from the decision of the Primary Examiner in an Office Action dated April 15, 2003, finally rejecting claims 22-38, all of the claims of the above-referenced application, and the Advisory Action dated July 3, 2003, denying Appellants' request for reconsideration.

Claims 22-38 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Schenk, WO 90/07351 in view of Velasquez, U.S. Patent No. 5,192,548. Claims 22, 23, 25, 26, 31 and 35 remain pending in the application as amended.

Appellants filed a Notice of Appeal on October 10, 2003, with the corresponding fee.

(4) STATUS OF AMENDMENTS

Appellants have filed with this brief an amendment canceling without prejudice or disclaimer claims 24, 26-30, 32-34 and 36-38. Claims 22, 23, 25, 26, 31 and 35, of which 22,

25, 31 and 35 are independent, remain pending in the application.

(5) SUMMARY OF INVENTION

The claimed invention provides methods for treating diabetes mellitus through the controlled inhalation of insulin powder. Effective diabetes treatment and the safety of the patient being treated both critically depend on the delivery of a consistent, repeatable and precisely controlled dose of insulin into the bloodstream of the patient. For this reason, treatment of diabetes has historically involved the injection of insulin, which permits the required consistency, repeatability and precision of insulin delivery to the bloodstream required for safe and effective diabetes treatment. General background regarding the disease of diabetes and the peculiarities of its treatment is provided in the patent application at paragraphs 0081-0085 and is recounted in part below.

Most diabetes patients would prefer to avoid insulin injections. Inhalation of insulin would provide a far more comfortable alternative approach to the treatment of the disease. But the mechanics and physiology of dosing insulin by inhalation differ vastly from those involved with the delivery of insulin by injection.

In the absence of Applicants' invention, insulin dosing by inhalation can be inconsistent. An important reason for this inconsistency is that the treatment of diabetes through inhalation of powdered insulin requires more than just delivery of a fixed dose to the patient's lungs. As the claims recite, it requires delivery of insulin to the lungs that allows delivery into the bloodstream of a controlled and repeatable dose. The key to successful and safe treatment is that the bloodstream – and not merely the lungs – receive the controlled, repeatable insulin dose. Inconsistencies in the dosing of insulin have serious and potentially dangerous consequences. Failure to deliver sufficient insulin into the bloodstream may cause a patient's blood glucose to

rise to a dangerously high level. Yet the delivery of too much insulin may cause the patient's glucose level to drop to a level that is dangerously low.

The inconsistency of delivery of insulin to the patient's bloodstream via inhalation, in the absence of Appellants' invention, has meant that patients must continue to dose themselves through injection.

Moreover, the prior art including the applied references contains no suggestion that other diseases treatable through drug inhalation can be analogized to diabetes in any relevant way. There is no suggestion in the art that diseases like asthma, a primary example of a disease treated by drug inhalation, either (1) require the delivery of the sort of consistent and controlled dose to the bloodstream of the patient required for insulin treatment of diabetes or (2) are susceptible of endangering the health or life of the patient if the inhaled dose and corresponding delivery to the bloodstream is not so consistent and controlled, as is the case with the injection of insulin. At most, the art shows that drugs and medications can be delivered into the lungs, but it stops there. The art does not show or suggest a method that results in controlled and repeatable delivery from the lungs into the bloodstream, which is critical for the safe and effective treatment of diabetes and is explicitly set forth in Applicants' claims.

Thus, despite the lack of any teaching or suggestion in the art, the present invention has at least in part addressed and overcome the difficulties associated with treating diabetes through inhalation. It has done so by providing a method for consistent, controlled and repeatable dosing of insulin to the patient's bloodstream though inhalation.

Among other features that are recited in the claims, the present invention includes a number of novel and nonobvious features. These features include:

(1) a method for treatment of diabetes mellitus involving supplying a predetermined or fixed amount of dry insulin powder for inhaled delivery via an inhalation device;

(2) creating an aerosolized suspension of insulin powder containing an amount of insulin that is greater, and in one aspect of the present invention 2-10 times greater, than the amount needed to be absorbed in the bloodstream of the patient being treated; and

(3) delivery of the insulin powder by inhalation at a flow rate and volume to allow the patient being treated to absorb in his or her bloodstream in a controlled quantity or dose to achieve acceptable blood glucose level following treatment, which in one aspect of the invention is between 1 and 50 units of insulin and in another aspect lowers the patient's blood glucose level to an acceptable value between 50 mg/dl and 300 mg/dl.

(6) ISSUES

The issues to be decided on appeal are:

1. Did the Examiner properly reject claim 22 under 35 U.S.C. § 103(a) as unpatentable over Schenk, WO 90/07351, in view of Velasquez, U.S. Patent No. 5,192,548?

2. Did the Examiner properly reject claim 23 under 35 U.S.C. § 103(a) as unpatentable over Schenk, WO 90/07351, in view of Velasquez, U.S. Patent No. 5,192,548?

3. Did the Examiner properly reject claim 25 under 35 U.S.C. § 103(a) as unpatentable over Schenk, WO 90/07351, in view of Velasquez, U.S. Patent No. 5,192,548?

4. Did the Examiner properly reject claim 26 under 35 U.S.C. § 103(a) as unpatentable over Schenk, WO 90/07351, in view of Velasquez, U.S. Patent No. 5,192,548?

5. Did the Examiner properly reject claim 31 under 35 U.S.C. § 103(a) as unpatentable over Schenk, WO 90/07351, in view of Velasquez, U.S. Patent No. 5,192,548?

6. Did the Examiner properly reject claim 35 under 35 U.S.C. § 103(a) as unpatentable over Schenk, WO 90/07351, in view of Velasquez, U.S. Patent No. 5,192,548?

(7) GROUPING OF CLAIMS

The pending claims are independent and do not stand or fall together. Appellants' claims will be argued in separate groupings as defined below:

Group I includes claims 22 and 23;

Group II includes claim 25 and 26;

Group III includes claim 31; and

Group IV includes claim 35.

(8) ARGUMENT

A. SUMMARY

The pending claims are directed to various aspects of a method for treating diabetes mellitus through the inhalation of powdered insulin. In rejecting these claims, the PTO has erred in several respects and has failed to make out a *prima facie* case of nonobviousness. First, in a blanket dismissal of various specific claim limitations, the PTO has invoked an "obvious to try" standard of patentability that is erroneous as a matter of law. Second, the PTO seeks to create an "implicit" or "inherent obviousness" standard which, too, has no basis in law. Third, the PTO has failed to point to any teaching or suggestion in the art of the invention *as a whole* including the specific limitations that are present in the pending claims. For example, each and every pending claim requires more than just mere controlled delivery of insulin to a patient's lungs; they explicitly require controlled absorption into the bloodstream, which in the absence of Applicants' disclosure would be unknown and would make treating diabetes with an inhaled powdered insulin unsafe and/or ineffective. For these reasons, Appellants urge the Board to reverse the rejection of the pending claims.

B. STATEMENT OF APPLICABLE LAW

1. Burden Is on the PTO to Establish *Prima Facie* Case of Obviousness

The burden is on the PTO to establish a *prima facie* showing of obviousness. In re Fritch, 972 F.2d 1260, 1265, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). A *prima facie* case of obviousness is established when the teachings from *the prior art itself* would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. In re Rijckaert, 9 F.3d 1531, 1532, 28 U.S.P.Q.2d 1955, 1956 (Fed. Cir. 1993)(emphasis added)(citations omitted). The appropriate test is "whether the claimed invention, considered as a whole, would have been obvious or nonobvious." Jones v. Hardy, 727 F.2d 1524, 1529, 220 U.S.P.Q. 1021, 1025 (Fed. Cir. 1984) (citations omitted). "Failure to consider the claimed invention as a whole is an error of law." Id. (citations omitted). Moreover, in seeking to establish a *prima facie* case of obviousness, the PTO may not rely on knowledge of Applicants invention to "pick and choose" among disclosures in the prior art to deprecate the claimed invention. In re Fine, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988).

2. "Obvious to Try" Is an Improper Basis of Rejection

Where, as here, the text of cited prior art references admittedly fails to disclose the limitations of the claimed invention as a whole, it is improper for the PTO to plug the gaps in its *prima facie* obviousness case by imagining what "one skilled in the art might find it obvious to try." Id. at 1075, 5 U.S.P.Q.2d at 1599. "[W]hether a particular combination might be 'obvious to try' is not a legitimate test of patentability." Id.; Jones, 727 F.2d at 1530, 220 U.S.P.Q. at 1026. The burden of establishing a *prima facie* case of obviousness cannot be met by arguing that the limitations of the claimed invention would have been "obvious to try" or could have been arrived at by "routine experimentation" or other language that erroneously overlooks how the invention as a whole is shown by the art. Whether or not the language "obvious to try" is

used by the PTO is not dispositive: the question remains whether the PTO has failed, in rejecting the claims, to consider the invention as a whole. In re Dien, 371 F.2d 886, 889, 152 U.S.P.Q. 550, 552 (C.C.P.A. 1967) (Smith, J., concurring).

3. Whether A Claim Element Is Inherent or Implicit in the Applied Prior Art References is Irrelevant to the Question of Obviousness

The PTO acknowledges, in the Advisory Action of July 3, 2003, that "Applicants argument alleging a lack of express disclosure of a treatment for diabetes is may be [sic] accurate; however, a treatment for diabetes is **implicit** in the express disclosure of the administration of powdered insulin inasmuch as insulin administration is known only for the treatment of diabetes." (Advisory Action at 3, emphasis added).

This is error. Consideration of an inherent quality is relevant only to anticipation, not obviousness. Jones, 727 F.2d at 1529-30, 220 U.S.P.Q. at 1025-26.

In a case analogous to the one presently before the Board, also involving methods of treatment, and one in which an "effective amount" of the use of a drug was claimed, a prior art disclosure of administering a drug to certain animals which did not *explicitly* disclose the limitations of the rejected claims as a whole, did not implicitly render obvious a claimed method of treating other animals by providing an "effective amount" of the drug for achieving a particular therapeutic purpose. In re Caldwell, 319 F.2d 254, 257-258, 138 U.S.P.Q. 243, 246-247 (C.C.P.A. 1963). As discussed in the summary above and in greater detail below, the treatment of diabetes and, more importantly, the methods of treatment claimed by the Applicants, require more than administration of insulin to a patient's lungs.

C. PRIOR ART REFERENCES AND BASIS FOR REJECTION

The primary applied reference, Schenk (PCT Publication WO 90/07351), relates to a device for delivering a drug to a patient by inhalation. Nowhere does Schenk refer to diabetes or

insulin or any other substance for use in controlling blood glucose. Schenk does not disclose or even suggest any recognition of a need to maintain any particular level of delivery of a drug to the bloodstream of a patient. Schenk also does not disclose any of the recited features of the claimed method, including those that are enumerated above in section (5).

The deficiencies of Schenk are said by the PTO to be supplied, in part, by Velasquez (U.S. Patent No. 5,192,548). Velasquez is relied on for the proposition that a blister pack can be made to contain insulin that can be inhaled using an inhalation device. Yet the reference makes only a single passing mention of insulin as the twentieth in a litany of approximately forty six drugs. No further mention is made either of the drugs or of anything relating to treatment of disease with any of them, including insulin.

Plainly, neither of the references relied on to reject the pending claims discloses or suggests anything relating to the treatment of diabetes using inhaled insulin, which – as the claims recite – requires more than merely depositing insulin into a patient's lungs; it also requires getting a precise, controlled and repeatable dose into the *bloodstream*. The PTO has openly acknowledged that the references, whether alone or in combination, do not mention the claim limitations such as are enumerated in section (5) above. Rather than address the invention as a whole, including these limitations, the PTO has instead overlooked those limitations and informed the Applicants in summary fashion that: "the amount of insulin employed and the amount absorbed can be arrived at through mere routine obvious experimentation and observation," (Office Action of April 15, 2003, page 3, rejecting claim 22) and would be "implicit in the express disclosure of the administration of powdered insulin." (Advisory Action of July 3, 2003, page 3). In the same fashion, the PTO contends that "it stands to reason that the administration protocol" – though it is not clear whose protocol – "would have included repeated inhalation (administration) of insulin to maintain an adequate concentration of

medicament in a patient's bloodstream." (Id. at 3 rejecting claim 23). No legal or factual bases for these blanket assertions has been provided.

D. TREATMENT OF DIABETES MELLITUS

Diabetes mellitus, as described above, is a disease requiring very carefully controlled delivery of insulin to the *bloodstream* of a patient. Until the present invention, adequate control of such delivery has demanded the use of injections. Insulin injections are known to be relatively precise and repeatable. Although this degree of control in the delivery of insulin is of therapeutic value for the patient and protects the patient from dangerous levels of dosing, the injection of insulin can be a source of patient discomfort. Yet there has been no effective alternative to this approach, despite its shortcomings.

Inhalation of insulin is potentially a vastly more comfortable delivery method than injection. But proper delivery of insulin to the bloodstream through inhalation, in the absence of the teachings of the present invention, is subject to dangerous inconsistency. It is not enough merely to deposit some known quantity of powdered insulin into the patient's lungs. The key to successful treatment requires consistent, repeatable absorption of a controlled dose into the patient's bloodstream. This depends on numerous factors, which the Applicants teach in their disclosure and among which are ones that Applicants have included in their claims. The art relied on by the PTO and the assumptions it has made in rejecting the claims, as discussed below, neither recognize this problem nor demonstrate a solution in the absence of the claimed teachings of the pending application.

E. THE PTO HAS NOT MET ITS BURDEN OF ESTABLISHING A *PRIMA FACIE* CASE OF OBVIOUSNESS

In rejecting the pending claims to a method of treatment of diabetes, as discussed in connection with Groups I-IV in sections H-K, below, the PTO has failed to establish a *prima*

facie case of obviousness. In failing to do so, the PTO has impermissibly overlooked its burden to consider the invention as a whole and to show, without the benefit of Applicants' own specification, how all of the limitations of the claims are shown by the prior art. The Schenk reference does not discuss, disclose or contemplate the treatment of diabetes. Nor does Velasquez, which merely identifies insulin as one among a number of drugs that can be placed in a blister pack. Even assuming, without conceding, that the Velasquez blister pack could be used with the Schenk device, that combination still does not disclose any method of treatment of diabetes, much less methods having the limitations of the claims as a whole. The PTO, in fact, has acknowledged that the "express" disclosure of the references fails to disclose the claimed invention. (Advisory Action of July 3, 2003 at 3).

F. THE REJECTIONS ARE BASED ON AN IMPROPER "OBVIOUS TO TRY" STANDARD

Rather than show how the invention as a whole is rendered obvious, the PTO has dismissed various specific claim limitations under an "obvious to try" standard of patentability that is erroneous as a matter of law. Fine, 837 F.2d at 1075, 5 U.S.P.Q.2d at 1599; Jones, 727 F.2d at 1530, 220 U.S.P.Q. at 1026; Dien, 371 F.2d at 889, 152 U.S.P.Q. at 552.

The PTO has stated (for example, in rejecting claim 22 (Group I)), that "[a]s to the recited intended result of the amount of insulin employed and the amount of insulin being absorbed, it is submitted that the amount of insulin employed and the amount absorbed can be arrived at through mere routine obvious experimentation and observation." (Office Action of April 15, 2003 at 3).

This is plainly an "obvious to try" basis for rejecting the claims, which fails to consider the claimed invention as a whole and is impermissible. It also erroneously substitutes the PTO's conjecture about the content of the prior art for the proper showing that the invention as a whole,

including all limitations, is in the prior art. Moreover, in the absence of any suggestion in the prior art of the claim as a whole the PTO's rejection has relied on the knowledge of Applicants' invention to "pick and choose" among the cited disclosures, and even to find disclosure in the art where none is actually present, in order to deprecate the claimed invention. As discussed below, the rejections of Groups II-IV, like the rejection of Group I, are similarly flawed.

G. THE REJECTIONS ARE BASED ON A MISPLACED "INHERENCY" STANDARD

When it dismissed Applicants' request for reconsideration of June 16, 2003, the PTO did so in reliance on an "implicit" or "inherent" obviousness standard. Ignoring the actual claim limitations, the PTO stated that "a treatment for diabetes is implicit in the express disclosure of the administration of powdered insulin." (Advisory Action of July 3, 2003, page 3). Such a standard has no basis in law. Jones, 727 F.2d at 1529-30, 220 U.S.P.Q. at 1025-26; Caldwell, 319 F.2d 254, 257-258, 138 U.S.P.Q. 243, 246-247. Invalidity due to inherent anticipation requires a showing that the PTO is neither entitled to make in an obviousness rejection, nor is able to make on the references before the PTO and the Board. A rejection based on this flawed application of the law must be reversed.

In the same fashion, the PTO contends that "is [sic, it] stands to reason that *the administration protocol* would have included repeated inhalation (administration) of insulin to maintain an adequate concentration of medicament in a patient's bloodstream.". (Id. at 3 rejecting claim 23, emphasis added). The PTO fails to identify any source for this "administration protocol" other than Applicants' own disclosure. Although its source is mysterious, the PTO appears here to have again engaged in an impermissible "obviousness-by-inherency" argument. Whether or not the unattributed administration protocol the PTO is relying

on would actually require repeated inhalation, no legal or factual bases for these blanket assertions has been provided.

H. GROUP I -- CLAIMS 22 AND 23

The PTO has failed to establish a *prima facie* case that the claims of Group I are obvious. These claims recite a method for treating diabetes mellitus in a patient by getting a controlled and repeatable dose of insulin into the patient's bloodstream via the patient's lungs. As discussed above, and as the PTO has essentially acknowledged, the applied prior art does not disclose any method for treating diabetes mellitus. It does not disclose or suggest the delivery of any drug into the bloodstream of a patient in a manner with precision and control as is required for insulin therapy of diabetics.

The Group I claims, however, include further specific limitations that the applied references also clearly fail to teach or suggest. Specifically, the Group I claims are limited to a method in which "the aerosolized suspension contains an amount of insulin that is 2-10 times higher than the amount needed to be absorbed in the bloodstream of the patient." As discussed in Section C, above, this limitation is also absent from the cited references, as is yet another limitation that requires "inhaling the aerosolized suspension at a flow rate and volume sufficient to allow the patient to absorb in the blood stream a controlled dose of insulin that comprises between 1-50 units of insulin."

Because the art relied on by the PTO fails to teach or suggest any method of treating diabetes mellitus, much less a method including all of the recited limitations of the claim as a whole, the PTO has failed to meet its burden of establishing a *prima facie* case of obviousness. Fritch, 972 F.2d at 1265, 23 U.S.P.Q.2d at 1783; Rijckaert, 9 F.3d at 1532, 28 U.S.P.Q.2d at 1956; Jones, 727 F.2d at 1528-29, 220 U.S.P.Q. at 1025; Fine, 837 F.2d at 1075, 5 U.S.P.Q.2d at 1598.

The rejection of the Group I claims on the grounds that the recited limitations, though admitted not to be explicitly shown in the art, would nevertheless have been (1) "obvious to try" or derived through "routine experimentation" or (2) "implicit" or "inherent" in the references, is predicated on legal as well as factual error and must be reversed. The law does not recognize an "obvious to try"/ "routine experimentation" standard for proof of obviousness under 35 U.S.C. § 103(a). Fine, 837 F.2d at 1075, 5 U.S.P.Q.2d at 1599; Jones, 727 F.2d at 1530, 220 U.S.P.Q. at 1026; Dien, 371 F.2d at 889, 152 U.S.P.Q. at 552. Nor does the law provide for "inherent" or "implicit" unpatentability under the obviousness statute. Jones, 727 F.2d at 1529-30, 220 U.S.P.Q. at 1025-26; Caldwell, 319 F.2d at 257-258, 138 U.S.P.Q. at 246-247. Still further, even if the PTO had not applied impermissible legal standards, it failed to establish the factual premises upon which its argument is grounded. For these reasons, the rejection of the claims of Group I is in error and should be reversed.

I. GROUP II -- CLAIMS 25 AND 26

The claims of Group II recite a repeatable method of regulating blood glucose in a human patient. Schenk and Velasquez, as the PTO has all but acknowledged, whether alone or in combination, do not disclose any method for regulating blood glucose, much less a repeatable method for doing so. A *prima facie* case of obviousness as to these claims has not been established.

The claimed method of regulating blood glucose includes further specific method step limitations that are neither taught nor suggested in the art: (1) in a repeatable manner, an aerosolized suspension of insulin inhaled by a patient practicing the method contains more insulin than is required in the bloodstream of the patient to achieve a satisfactory blood glucose level, and (2) at least a portion of the aerosolized suspension of insulin is flowed through a mouthpiece on the device and into the lungs of the patient in a manner sufficient to cause the

patient to absorb in the patient's bloodstream a sufficient, controlled quantity of insulin to achieve acceptable glucose level following treatment. The absence of any teaching or suggestion of these method limitations further establishes the failure of the PTO to establish a *prima facie* case of nonobviousness. Fritch, 972 F.2d at 1265, 23 U.S.P.Q.2d at 1783; Rijckaert, 9 F.3d at 1532, 28 U.S.P.Q.2d at 1956; Jones, 727 F.2d at 1528-29, 220 U.S.P.Q. at 1025; Fine, 837 F.2d at 1075, 5 U.S.P.Q.2d at 1598.

In the Office Action of April 15, 2003, the PTO stated, incorrectly, that Schenk as modified by Velasquez "teaches flowing at least a portion of the aerosolized suspension through a mouthpiece (20) on the device and into the patient's lungs in a manner sufficient to cause the patient to absorb a controlled quantity of insulin." (Office Action of April 15, 2003 at 3). No citation is provided by the PTO in support of this assertion, because the references disclose nothing of the sort. All but acknowledging the defects in its obviousness argument in denying Applicants' request for reconsideration, the PTO revised the basis for its rejection. Its new position was that "a treatment for diabetes is implicit in the express disclosure of the administration of powdered insulin." (Advisory Opinion of July 3, 2003 at 3).

This newly articulated basis of rejection is flawed in several respects. First, whether the references are taken alone or in combination, there is no express disclosure of the administration of powdered insulin. Assuming, without conceding, that there were such a disclosure, this basis for rejection is still inappropriate because it ignores the limitations of the claims as a whole and relies on a flawed legal theory of "implicit" or "inherent" obviousness. Jones, 727 F.2d at 1529-1530, 220 U.S.P.Q. at 1025-26; Caldwell, 319 F.2d at 257-258, 138 U.S.P.Q. at 246-247.

For each of these reasons, the rejection is improper and must be reversed.

J. GROUP III – CLAIM 31

The claim of Group III recites a repeatable method of lowering a patient's serum glucose level to acceptable value. As with Groups I and II, because the applied art neither discloses nor suggests such a method, the PTO has failed to establish a case of *prima facie* obviousness. Fritch, 972 F.2d at 1265, 23 U.S.P.Q.2d at 1783; Rijckaert, 9 F.3d at 1532, 28 U.S.P.Q.2d at 1956; Jones, 727 F.2d at 1528-29, 220 U.S.P.Q. at 1025; Fine, 837 F.2d at 1075, 5 U.S.P.Q.2d at 1598. In fact, claim 31 also recites inhaling at least a portion of the suspension (of dry insulin powder) at a flow rate and volume sufficient to deposit a sufficient, controlled quantity of insulin in the patient's lungs so that the patient absorbs into the blood between 1 and 50 units of insulin, thereby lowering the patient's blood glucose level to an acceptable value between 50 mg/dl and 300 mg/dl. These limitations are also entirely absent from the combined disclosures of Schenk and Velasquez, underscoring the PTO's failure to meet its burden. Significantly, the combined disclosures do not address the importance of precision and control of the dose absorbed into the bloodstream. They are merely concerned with getting a drug into a patient's lungs.

The PTO presented the same argument as it had for claims 22 and 23 (Group I), which Applicants have addressed above. The PTO also argued as follows: "Given that Schenk et al. disclose aerosolizing most of the medicament within the aerosolization chamber (16), the amount of medicament available for inhalation by a patient is predictable." (Amendment of April 15, 2003 at 4). Whether or not this pronouncement is true, it bears little if any relevance to the specific limitations regarding absorbing into the blood between 1 and 50 units of insulin and the consequent lowering of the patient's blood glucose level to an acceptable value between 50 mg/dl and 300 mg/dl. These are highly specific limitations, which are in no way met by the basis for the rejection given by the PTO in the Office Action.

As with Groups I and II, the PTO summarily denied the request for reconsideration on the grounds that the claim limitations are "implicit" in the combined references. (Advisory Action of July 3, 2003 at 3). For the reasons presented above in connection with Groups I and II, this basis for rejecting claims is erroneous as a matter of law, Jones, 727 F.2d at 1529-1530, 220 U.S.P.Q. at 1025-26; Caldwell, 319 F.2d at 257-258, 138 U.S.P.Q. 246-247, and is unsupported in fact For all of these reasons, the rejection of claim 31 is improper and should be reversed.

K. GROUP IV – CLAIM 35

The claim of Group IV is directed to a method of administering insulin to a diabetic patient to control serum glucose levels via a hand held inhalation device. As discussed above, Schenk and Velasquez do not disclose any method of administering insulin to a diabetic patient's bloodstream to control serum glucose levels and, for this reason alone, the rejection has failed to establish a *prima facie* case of obviousness. Fritch, 972 F.2d at 1265, 23 U.S.P.Q.2d at 1783; Rijckaert, 9 F.3d at 1532, 28 U.S.P.Q.2d at 1956; Jones, 727 F.2d at 1528-29, 220 U.S.P.Q. at 1025; Fine, 837 F.2d at 1075, 5 U.S.P.Q.2d at 1598. At most the combination of Schenk and Velasquez would disclose the possibility of delivering insulin into the patient's lungs, which in itself is not a method of treatment of diabetes and certainly not the method Applicants have claimed with all its limitations.

Claim 35 also recites several additional limitations, none of which are taught or suggested by the references whether taken alone or in combination. Claim 35 includes a limitation that a cloud of air and suspended insulin particles be formed in a quantity having 2-10 times the dosage of insulin required to be delivered into the patient's blood to achieve acceptable glucose level.

Schenk and Velasquez clearly disclose nothing of the sort.

The PTO's bases for rejecting claim 35 and denying Applicants' request for reconsideration are identical to those given for claim 31, which is telling, since the limitations in

the two claims differ greatly from one another. In response to these bases, Applicants refer to, and incorporate into this section, their relevant arguments from above, including those of Section J addressing the rejection of claim 31.

In short, the PTO has failed to demonstrate that the prior art discloses the invention as a whole, and has impermissibly relied on an "obvious to try"/"routine experimentation" rejection, Fine, 837 F.2d at 1075, 5 U.S.P.Q.2d at 1599; Jones, 727 F.2d at 1530, 220 U.S.P.Q. at 1026; Dien, 371 F.2d at 889, 152 U.S.P.Q. at 552, buttressed by a legally erroneous "implicit"/"inherent" obviousness argument. Jones, 727 F.2d at 1529-1530, 220 U.S.P.Q. at 1025-26; Caldwell, 319 F.2d at 257-258, 138 U.S.P.Q. at 246-247.

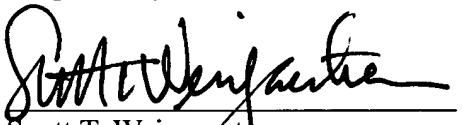
For these reasons, the rejection of claim 35 should be reversed.

(9) CONCLUSION

Applicants respectfully submit that, for the reasons given above, claims 22, 23, 25, 26, 31 and 35 were improperly rejected as obvious and are allowable over the cited art. The PTO has erred. Applicants request reversal of the rejection.

Dated: May 10, 2004

Respectfully submitted,



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APPENDIX OF CLAIMS

22. A method for treating diabetes mellitus in a patient comprising the steps of:

a. supplying a predetermined amount of dry insulin powder to an inhalation device;

b. releasing a pressurized gas over the predetermined amount of dry insulin powder to create an aerosolized suspension comprising powder suspended in air, wherein the aerosolized suspension contains an amount of insulin that is 2-10 times higher than the amount needed to be absorbed in the bloodstream of the patient; and

c. inhaling the aerosolized suspension at a flow rate and volume sufficient to allow the patient to absorb in the bloodstream a controlled dose of insulin that comprises between 1-50 units of insulin.

23. The method of claim 22, wherein steps a-c may be repeated periodically as needed to treat the patient and wherein the amount of insulin supplied to the bloodstream in step c remains relatively constant for each repetition of steps a-c.

25. A repeatable method of regulating blood glucose levels in a human patient, the method comprising the steps of:

a. supplying a fixed quantity of dry insulin powder to a portion of a hand held inhalation delivery device;

b. propelling a gas over the fixed quantity of dry powder to produce, in a repeatable manner, an aerosolized suspension of insulin, the aerosolized suspension

containing more insulin than is required in the bloodstream of the patient to achieve a satisfactory blood glucose level; and

c. flowing at least a portion of the aerosolized suspension through a mouth piece on the device and into the lungs of the patient in a manner sufficient to cause the patient to absorb in the patient's bloodstream a sufficient, controlled quantity of insulin to achieve acceptable blood glucose level following treatment.

26. The method of claim 25, wherein steps a-c may be repeated periodically as needed to treat the patient and wherein the amount of insulin supplied to the bloodstream in step c remains relatively constant for each repetition of steps a-c.

31. A repeatable method of lowering a patient's serum glucose level to acceptable value, the method comprising the steps of:

a. supplying a predetermined amount of dry insulin powder to a medical device;

b. releasing a compressed gas over the dry insulin powder to form a suspension comprised of dry insulin powder and air; and

c. inhaling at least a portion of the suspension at a flow rate and volume sufficient to deposit a sufficient, controlled quantity of insulin in the patient's lungs so that the patient absorbs into the blood between 1 and 50 units of insulin, thereby lowering the patient's blood glucose level to an acceptable value between 50 mg/dl and 300mg/dl.

35. (Amended) A method of administering insulin to a diabetic patient to control serum glucose levels via a hand held inhalation device, the method comprising the steps of:

a. supplying a predetermined quantity of insulin powder to a portion of the device;

b. aerosolizing the insulin powder to form a cloud of insulin within the device, the cloud comprised of air and suspended insulin particles, the quantity of insulin particles being 2-10 times the dosage of insulin required to be delivered into the patient's blood to achieve acceptable blood glucose level;

c. administering to the patient's bloodstream via the patient's lungs a sufficient controlled and repeatable quantity of insulin from the cloud to produce an acceptable blood glucose level in the patient.